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EXAMINER
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SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
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1635

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06/01/2011

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/564,707	<b>Applicant(s)</b> HATZIGEORGIOU ET AL.
	<b>Examiner</b> RICHARD SCHNIZER	<b>Art Unit</b> 1635

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 April 2011.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 12-22 and 27-38 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12-22 and 27-38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

The Examiner in charge of this Application has changed. Please direct further correspondence to Richard Schnizer, whose contact information is given at the end of the action.

An amendment was received and entered on 4/19/2011.

Claims 33-38 were added.

Claims 12-22 and 27-38 are pending.

Rejections not reiterated are withdrawn.

### ***Claim Objections***

Claims 16-19 are objected to for their recitation of "claims 12". Substitution of the singular "claim" for the plural "claims" is suggested.

Claims 14 and 15 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. In claim 14, the limitation "wherein a free energy determination of -20 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for microRNA" does not further limit claim 12 because it does not contain any active method step for determining free energy. Moreover, the claim language is open and does not indicate that binding pairs with a free energy of greater than -20 kcal/mol are not indicative of a miRNA-MRE relationship. Claim 15 has a similar deficiency. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Similarly, claims 34 and 35 are objected to for failing to further limit claim 33.

The language indicating that a free energy determination of -20 or -30 kcal/mol indicates that the target mRNA sequence is a MRE for the generated miRNA is open language. Therefore it exclude binding pairs with a free energy of greater than -20 kcal/mol from the genus of binding pairs in a miRNA-MRE relationship required by the claims.

Claim 22 is objected to for its recitation of the phrase “a computer system that for identifying a microRNA oligonucleotide sequence”. Deletion of “that” is suggested.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-22, 27, and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12-22, 27, and 28 are indefinite in their description of the mRNA in item 'b)' of the claims. In this passage, the claims recite an embodiment in which "the mRNA has 0 nucleotides when the loop region of the microRNA is 6-9 nucleotides". This renders the claim indefinite because if the mRNA had 0 nucleotides, then there would be no mRNA.

Claim 16 is indefinite in its recitation of “the selected mRNA sequence is a known MRE.” The genus of “known” MREs is subject to change as new MREs are

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discovered. Thus the metes and bounds of the claims are subject to change over time, and one cannot know what is embraced by the claims and what is not.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Based upon consideration of all of the relevant factors with respect to the claims as a whole, claim(s) 12-18, 22, 31, and 32 are held to claim an abstract idea, and is/are therefore rejected as ineligible subject matter under 35 U.S.C. 101. The rationale for this finding is explained below:

The subject matter of claims 12-18, 31, and 32 is a process of generating a nucleotide sequence. Factors weighing against eligible subject matter are:

- 1) no recitation of a machine or transformation (either express or inherent)
- 2) the claim is not directed toward applying a law of nature
- 3) the claim is a mere statement of a general concept.

The claimed subject matter is not limited to use a particular apparatus or machine in the steps of the method. The claimed process does not transform an article to a different state or thing because there is no synthetic step in which an miRNA, or any oligonucleotide, is actually made. All that is necessarily generated is the idea of a sequence of nucleotides. The claimed subject matter does not require that the steps of the method are actually performed on a machine or in a more tangible, concrete fashion resulting in a transformation of matter. Preamble limitations, such as “generating a

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microRNA” will not be considered sufficient to convert into statutory subject matter a process that does not otherwise require steps that are performed on a machine or that transform matter. The claimed process does not include an explicit application of a law of nature (i.e. a principle deduced from facts that always occurs) in more than a nominal, insignificant, or tangential way. The claimed process requires use of a general concept. Amendment to include limitations within the steps of the method that require use of a machine, such as using a computer to execute the method steps, or that require a transformation of matter, as in instant claims 27, 28, 29, 30, and 33-38, will overcome the above rejection. The applicants are cautioned against introduction of new matter in an amendment.

Regarding claim 22, the claimed subject matter is a computer program on a computer readable medium. A review of the specification did not reveal any definition of computer readable media that excludes an embodiment that is information in a signal. As such, an embodiment of the claims reads on non-statutory subject matter (In re Nuijten 84 USPQ2d 1495 (2007)). The applicants may overcome the rejection by 1) amendment of the claims to be limited to physical forms of computer readable storage media described in the specification or 2) by amending the claimed subject matter to be limited to “non-transitory”. See the notice regarding Computer Readable Media (1351 OG 212 (23 February 2010)). This notice sets forth the basis of the rejection above, but also states the following with regard to amendments to include the phrase “non-transitory” and the prohibition against adding new matter:

A claim drawn to such a computer readable medium that covers both transitory and non-transitory embodiments may be amended to narrow the claim to cover only statutory embodiments to avoid a rejection under 35 U.S.C. § 101 by adding the limitation “non-transitory” to the claim. Cf. *Animals* -

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Patentability, 1077 Off. Gaz. Pat. Office 24 (April 21, 1987) (suggesting that applicants add the limitation "non-human" to a claim covering a multi-cellular organism to avoid a rejection under 35 U.S.C. § 101). Such an amendment would typically not raise the issue of new matter, even when the specification is silent because the broadest reasonable interpretation relies on the ordinary and customary meaning that includes signals per se. The limited situations in which such an amendment could raise issues of new matter occur, for example, when the specification does not support a non-transitory embodiment because a signal per se is the only viable embodiment such that the amended claim is impermissibly broadened beyond the supporting disclosure. See, e.g., *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473 (Fed. Cir. 1998).

### ***Response to Arguments***

A rejection similar to the one set forth above was previously set forth in the action of 4/13/2010, and was withdrawn in the Action of 12/17/2010. After further consideration and consultation, the rejection is reinstated as set forth above. Applicant's arguments against the rejection, filed 10/5/2010 have not been considered previously, but are fully considered below and are not persuasive.

Applicant argued that the Supreme Court recently rejected the Federal Circuit "machine-or-transformation test" as too narrow, indicating that this was not the sole test for deciding whether an invention is a patent-eligible process. Applicant concludes that the instantly claimed process is therefore patentable.

This is unpersuasive because the "machine-or-transformation test" is not the sole factor considered in the rejection above. As stated above, other factors were considered as well, including whether or not the claim is directed to the application of a law of nature, and whether the claim is more than a mere statement of a concept. The conclusion that the process is not patent eligible was based on consideration of each of these factors, not solely on the machine-or-transformation test, in accordance with the

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Interim Guidance for Determining Subject Matter Eligibility for Process Claims in view of *Bilski v. Kappos* (Fed. Reg. 75(143): 43922-43927, 7/27/2010).

Applicant also argued that “generation of a microRNA is not abstract”, and that the step of generating an oligonucleotide sequence that is 17-25 nucleotides and has a degree of complementarity to the selected mRNA sequence that is indicative of a microRNA-recognition element for microRNA. The Office disagrees. In the absence of an active step of synthesis, all that is generated is the idea of a miRNA, i.e. a string of letters which is an abstraction of an actual, physical miRNA. For these reasons the rejection is reinstated.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.



Claims 12-18, 27-30, and 33-38 are rejected under 35 U.S.C. 102(a) as being anticipated by Doench et al (Genes Dev. 18: 504-511, 1/2004, of record).

Doench investigated the structure and function of miRNAs, in particular the free energy of binding between the miRNA and the target mRNAs. Reporter constructs were prepared comprising a luciferase open reading frame with known miRNA binding sites (instant claim 16) in the 3'UTR (instant claims 17 and 36). Various miRNAs were constructed (instant claim 18) and paired with sense strands to make siRNAs comprising an miRNA as an antisense strand. These constructs were used to transfect cells comprising the reporter constructs, and expression of luciferase was measured (instant claims 27, 29, and 37). Fig. 1A shows one such miRNA, depicted as an siRNA antisense strand, hybridized to a target mRNA. It consists of a 5' region of 8 nucleotides perfectly paired to the mRNA, a loop region of 3 nucleotides opposite an unpaired mRNA region of 2 nucleotides, and a 3' region of 10 nucleotides perfectly paired to the mRNA, thus satisfying the structural requirements for the miRNA and its relationship to the mRNA in instant claims 12 and 29. This miRNA repressed target gene expression 12-fold (instant claims 28, 30, and 38). See Fig. 8B and 2C on page 507.

Regarding claims 13, 33, and 34, Doench measured the binding energies of the 5' and 3' miRNA regions, thereby satisfying the limitations that require "determining free energy of the microRNA bound to the selected mRNA sequence" and "determining free energy of a microRNA oligonucleotide sequence bound to the selected mRNA sequence". See Fig. 2C. The first structure in Fig. 2C is the miRNA/mRNA pair from

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Figure 1A. The third structure in the left column of Fig. 2C also comprises an miRNA strand that meets the limitations of the rejected claims. It is noted that while claim 33 indicates that mRNA regions with binding energies of -10 kcal/mole or less for a given miRNA are considered to be MREs for that miRNA, the claim language is open and does not exclude mRNA regions with binding energies of greater than -10 kcal/mol from being MREs for the miRNA. Thus mRNA targets with complementarity to the miRNA that provides a binding energy of greater than -10 kcal/mol are not excluded by the claim from being a micro-RNA recognition element for the recited miRNAs

Claim 14 is included in the rejection because the phrase “wherein a free energy determination of -20 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for microRNA” carries no patentable weight since it does not limit the claim in any way. That is, the claim requires no step of measuring free energy of binding, so the language regarding binding energy determination carries no weight. Moreover, while the claim indicates that mRNA regions with binding energies of -20 kcal/mole or less for a given miRNA are considered to be MREs for that miRNA, it does not exclude mRNA regions with binding energies of greater than -20 kcal/mol from being MREs for the miRNA. Claims 15, 34, and 35 are included for the same reasons.

Thus Doench anticipates the claims.

Claims 12, 14-18, 27, and 28-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Zeng et al (RNA 9: 112-123, 2003).

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Zeng studied the sequence requirements for miRNA processing and function. An expression vector encoding chloramphenicol acetyl transferase was constructed and 4 known target sites for miR-30 were inserted into the 3' UTR. An expression vector for miR-30 was constructed and miR-30 was expressed as a precursor that was processed to a mature miRNA. See Fig. 2 on page 115, which also shows the relationship between miR30 and its target is shown in Fig. 2 on page 115. MiR-30 consists of a 5' region of 9 nucleotides perfectly matched to the target, 2 unpaired nucleotides opposite 3 unpaired nucleotides in the target, and a 3' region comprising 10 nucleotides perfectly matched to the target. The miRNA suppressed target gene expression by about 85 percent (Fig. 2).

Claim 14 is included in the rejection because the phrase “wherein a free energy determination of -20 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for microRNA” carries no patentable weight since it does not limit the claim in any way. That is, the claim requires no step of measuring free energy of binding, so the language regarding binding energy determination carries no weight. Moreover, while the claim indicates that mRNA regions with binding energies of -20 kcal/mole or less for a given miRNA are considered to be MREs for that miRNA, it does not exclude mRNA regions with binding energies of greater than -20 kcal/mol from being MREs for the miRNA. Claim 15 is included for the same reasons.

Thus Zeng anticipates the claims.

Claims 12-17, and 31 are rejected under 35 U.S.C. 102(e) as being anticipated by Bentwich (US 7250496), taken with the evidence of Tinoco et al (Nature New Biology 246(4): 40-41, 1973, of record).

Bentwich taught methods of bioinformatically detecting miRNAs and their binding sites in which a bioinformatic gene detection engine is trained to recognize known miRNA genes by hairpin detector training and validation, to identify dicer cleavage locations, and to detect target-gene binding-sites in an untranslated region of a target mRNA. To identify target sites, a target site detector receives as input a plurality of identified dicer-cut sequences (miRNAs), and a plurality of potential target gene sequences (mRNAs). Target-genes having binding site(s) with a nucleotide sequence which is at least partially complementary to that of the dicer-cut sequences are identified

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as follows. The target-gene binding-site detector first performs a BLAST comparison of the nucleotide sequence of each of the plurality of dicer-cut sequences, to the potential target gene sequences, in order to find crude potential matches. Blast results are then filtered to results which are similar to those of known binding sites (e.g. binding sites of miRNA genes Lin-4 and Let-7 to target genes Lin-14, Lin-41, Lin 28 etc.). Next the binding site is expanded, checking if nucleotide sequences immediately adjacent to the binding site found by BLAST, may improve the match. Suitable binding sites, then are computed for free-energy and spatial structure. The results are analyzed, selecting only those binding sites, which have free-energy and spatial structure similar to that of known binding sites. Identified miRNAs and genes are confirmed empirically with wet lab experiments. See column 13, line 60 to column 17, line 48, especially at column 13, line 60 to column 14, line 14; column 15, lines 26-52; column 16, lines 4-17; and column 17, lines 8-48.

Using this system, Bentwich generated several miRNA sequences that recognize targets in 3' untranslated regions of genes. Figs. 26-28 show DNA versions of such miRNAs paired with DNA versions of mRNA binding sites.

See for example Fig. 26D/41 (drawing sheet 74 of 148). Note that the fourth miRNA/target pair (defined by SEQ ID NO: 20604 and SEQ ID NO: 362996) satisfies the limitations of claim 12 wherein the miRNA comprises 22 nucleotides, the miRNA has a proximal 5' region of 8 nucleotides that is perfectly paired with the target, the miRNA has a loop region of 0 nucleotides that is opposite an unpaired target loop of 3

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nucleotides, and the miRNA has a distal region of 14 nucleotides, including 9 consecutive nucleotides that are perfectly paired to the target, as shown below.

			---		---	
miRNA	5'	TCGCCGCC		ACCGCCGCC		GCCGC 3'
BINDING SITE	3'	AGCGGCGG		TGGTGGCGG		CGGCG 5'
			CAG		CAA	

It is noted that the binding energy of the RNA version of this pair is less than -30 kcal/mol in view of the rules of Tinoco (see page 41). Thus the method of Bentwich was used to generate a microRNA of 22 nucleotides that meets the limitations of instant claims 12, 17, and 31.

See also Fig. 26D/3 (drawing sheet 36 of 148). The first miRNA/target pair, defined by SEQ ID NOS: 20604 and 69717 satisfies the limitations of claim 12 wherein the miRNA comprises 22 nucleotides, the miRNA has a proximal 5' region of 8 nucleotides that is perfectly paired with the target, the miRNA has a bulge of 3 nucleotides opposite a 3 nucleotide bulge in the target, and the miRNA has a distal region of 11 nucleotides, a mismatch of 1 nucleotide flanked by two runs of 5 nucleotides that are complementary to target, as shown below.

			ACC		C	
miRNA	5'	TCGCCGCC		GCCGC	GCCGC	3'
BINDING SITE	3'	GGCGGCGG		CGGCG	CGGCG	5'
			CGA		A	

The binding energy of the RNA version of this pair is less than -30 kcal/mol in view of the rules of Tinoco.

Claim 13 is included in this rejection because Bentwich taught a method step in which free energy of miRNA/mRNA target pairs was calculated. It is noted that the

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claim language “wherein a free energy determination of -10 kcal/mole or less indicates that said mRNA sequence is a microRNA- recognition element for the microRNA” is open, and does not result in a limitation in which any mRNA/miRNA pair with a binding energy of greater than -10 kcal/mole is discarded.

With regard to claims 14, it is noted that the phrase “wherein a free energy determination of -20 kcal/mole or less indicates that said mRNA sequence is a microRNA-recognition element for microRNA” carries no patentable weight since the claim requires no step of measuring free energy of binding. Moreover, while the claim indicates that mRNA regions with binding energies of -20 kcal/mole or less for a given miRNA are considered to be MREs for that miRNA, it does not exclude mRNA regions with binding energies of greater than -20 kcal/mol from being MREs for the miRNA. Claim 15 is similar in this regard.

Claim 16 is included in the rejection because the mRNA binding site has the structural characteristics of an MRE, and it is “known” because it is disclosed.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 12-22, 27, 29-31, and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bentwich (US 7250496).

The teachings of Bentwich are discussed above. These teachings anticipate, and therefore render obvious, claims 12-17, and 31.

With regard to instant claims 18, 27, 29, 33, and dependents, and limitations requiring synthesis of an miRNA oligonucleotide, Bentwich did not disclose the actual synthesis of the miRNAs relied on in the rejection above (those disclosed in Figs. 26D/3 and 26D/41). However, Bentwich taught that the functions of the identified miRNAs and targets should be confirmed empirically. See column 14, lines 8-16. Moreover, since the intended purpose of the method is to detect functional miRNAs and targets, it is clear that one of ordinary skill would have been motivated to test the identified miRNAs. Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to synthesize and test the miRNAs against the predicted target sequences.

Instant claims 19-21 are drawn to a system for identifying a microRNA-recognition element comprising: an input interface for inputting mRNA sequences, a database of mRNA sequences or a link for connecting to a remote data input interface, data or a database of mRNA sequences; an input interface for inputting microRNA sequences, a database of microRNA sequences or a link for connecting to a remote data input interface, data or a database of microRNA sequences; a processor with instructions for comparing mRNA sequences to microRNA sequences to identify a microRNA-recognition element according to the method of claims 12.

Bentwich clearly intended that the disclosed method could be carried out by a computer system (see e.g. Fig. 10 and its brief description). Accordingly, in order to



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input a plurality of identified dicer-cut sequences (miRNAs), and a plurality of potential target gene sequences (mRNAs), as described at column 17, lines 18-28, it is clear that the system must have an input interface for each of these purposes, as well as a processor with instructions (i.e. a computer and a program) for carrying out the method. Thus Bentwich accounts for the limitations of claims 19, 21, and 22.

Regarding claim 20, Bentwich did not clearly teach a link for connecting to a database of mRNA sequences. However, at column 12, lines 30-39, Bentwich indicated that expressed RNA data to be used in the invention may be obtained from the National Center for Bioinformatics (NCBI) or from the Online Mendelian Inherited Disease In Man (OMIM) database. As it was routine in the art at the time of the invention for computers to be linked to the internet, and therefore to a variety of web databases such as those provided by NCBI and OMIM, it would have been obvious for the system of Bentwich to have a link for connecting to these databases.

Regarding claims 34 and 35, and the recitation that a free energy determination of -20 or -30 kcal/mol indicates that the target mRNA sequence is a MRE for the generated miRNA, it is reiterated that this recitation does not further limit the claims, and so claims 34 and 35 are obvious for the same reasons applied to claim 33.

The limitations of claims 36 and 37 are addressed above under 35 USC 12 rejections. The method of Bentwich is designed to detect target sequences in the 3' UTR (see e.g. Figs. 24A, 25A, 26A, 27A, and 28A). Moreover, Bentwich suggests that the miRNAs and targets should be tested empirically, and one of ordinary skill would have been motivated to do so in any event.

Thus the invention as a whole was prima facie obvious.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's acting supervisor, Heather Calamita, can be reached at (571) 272-2876. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Richard Schnizer/  
Primary Examiner, Art Unit 1635